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Addressing Challenges in Sustainable Vaccine Productions and R&D industry's Views on Technology Transfer

HHS-WHO International Vaccine Technology Workshop

Hyderabad, India (17-18 September 2010)

Michel Baijot (GSK) on behalf of IFPMA

Poverty: a broad issue

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- in 2009, 1.4 billion people lived on less than $4 a day
- A billion people don't have access to drinking water
- A billion people suffer from hunger
- Nearly one million people die each year of malaria, 1.8 million of tuberculosis, and 2 million of AIDS
- Poverty keeps some 72 million children out of school and prevents them from realizing their potential

Heathcare for All: a public health failure?

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- In 2009:
  - 30,000 children under 5 years of age die every day, mainly due to dehydration, undernourishment, and vaccine-preventable diseases
  - About a third of the world's population lacks adequate access to quality of health care, including vaccines
- Gaps in Immunization
  - Nearly 30 million children born every year are not fully immunized
  - DTP vaccination rate in Africa has lowered around 50% over the past 15 years
  - Before GAVI, it often took 10-20 years before the introduction of "new vaccines" in developing countries
  - Lack of investment in vaccines against diseases prevalent in developing countries (so called "neglected diseases")

Factors Affecting Access to Healthcare & Vaccines

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- Underlying general situation
  - Poverty
  - Political stability (wars and conflicts)
  - Political willingness (& corruption)
  - Cultural barriers

- Programmatic factors:
  - Lack of health infrastructure (health care system and logistics)
  - Lack of precise policy plans & long-term forecasting
  - Financial (pricing & reimbursement, distribution costs)
  - Capacity building
  - Regulatory issues (requirements, review timelines)

Technology Transfer is not the only factor that impacts access to care and to vaccines

Addressing Challenges in Sustainable Vaccine Production

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An effective response to healthcare challenges and access to vaccines in the developing world embraces many elements including:

- Political will
- Improved healthcare infrastructure
- Appropriate industrial policy solution
- Affordability of the product
- Funding

Definition of Technology Transfer

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- What is Technology Transfer?*
  - Transfer of skills, knowledge, technologies, methods of manufacturing, quality management systems, samples of manufacturing and facilities
- To whom
  - Within or outside an organization, a geography or an industry/discipline/sector
- Why
  - To increase access to scientific and technological developments
  - To allow further development/adaptation and exploitation of the technology into new products, processes, applications, materials or services
- However,
  - In some circumstances, Tech transfer is a condition imposed by governments on companies seeking to supply products in their countries

*Adapted from http://en.wikipedia.org/wiki/Technology_transfer

Types of Technology Transfer

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- A wide range of health-related technologies can be transferred to developing countries:
  - R&D capacity
  - Clinical trials
  - Laboratory testing
  - Quality assessment
  - Supply chain management and logistical issues
  - Training of personnel is crucial
  - Information technology systems
  - Project / human resource management
  - Local production
- Many of these are not solely in the remit of industry

Technology Transfer is Considered by Different Stakeholders as a way to:

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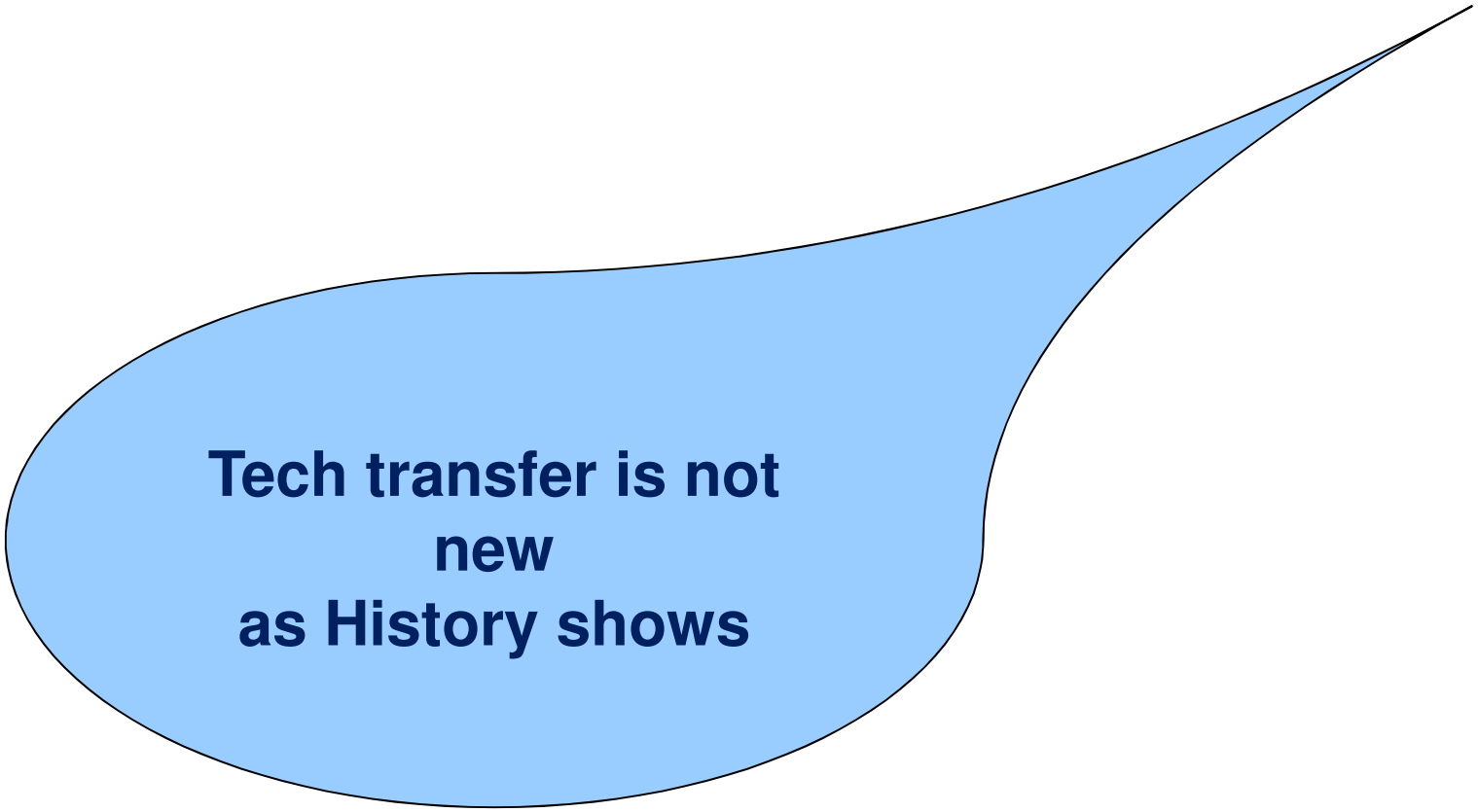
1. Increase vaccine access and capacity
2. Lower Cost of Goods
3. Increase employment and wealth
4. Stimulate local industry and entrepreneurship
5. Share Know-How
6. Share Intellectual Property

In essence:
Give a man a fish, he'll eat for a day!
Teach a man to fish, he'll eat for lifetime


Tech transfer is not
new
as History shows

Four Eras of Vaccination, Four Eras of Tech Transfer

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Vaccine Tech Transfer has mirrored the Vaccine industry evolution

1. **Heroic era (before1930s)**
   - Heroically led artisanal revolutions
2. **National public health (1930s ➞ 1990s)**
   - National vaccine institutes
   - Growing complexity, sophistication and regulations
   - Divergence between Developed and Developing World
3. **Global vaccination programs (1960s ➞ 2000s)**
   - Smallpox, Polio
   - UNICEF, EPI, CVI, GAVI
4. **Era of privatization and biotechnology (~1990 ➞ to date)**
   - Rapid reduction in number of national and commercial producers
   - Future supply and innovation from unsubsidized producers dependant on:
     - Know-how and appropriated IP
     - Sustainability/ profit (price, quantity and cost of goods)

1. Heroic Era (before 1930s)

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- Low-Tech/Artisanal → Low cost
- Low or No Regulatory Hurdles
- No or Low Quality Standards
- Tech Transfer by Single Person Study/Communication

Making yellow fever vaccine ……probably

Smallpox (Vaccinia) vaccine

2. Era of National Public Health Institutes Involvement (1930s ➡ 1990s)

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But Rapid Divergence Between Developed Countries……

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- **New vaccines**
  - Polio (Salk & Sabin)
  - Measles
  - Mumps
  - Hepatitis B
  - Meningococcus
  - Haemophilus influenza
  - Combinations
- **New technologies**
  - Culture on chick embryos (Goodpasture, Walter Reed, 1931)
  - Tissue culture (Enders, 1949)
  - Recombinant vaccines (1980s)
  - Conjugate vaccines (1980s)
  - Plus improved production and assay techniques
- **New regulations**
  - "Jim" and Biologicals Act:1902
  - Cutter incident: 1955, led to creation of Division of Biologics Standards in NIH, now FDA
  - GMP and management of input materials 1963 and 1976
  - Management of air pressure – 1978/87
  - WHO developed a prequalification system – 1989(?)
  - Documentation and Team Biologics -1990s
  - Many more regulatory and quality standards

……and Less Developed Countries

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- Many small scale producers, e.g., 74 rabies vaccine producers in 1984
- Frequent GMP problems
- Did not make new vaccines
  - OPV, not IPV
  - Whole-cell pertussis, not acellular
- Independence and conversion of colonial public health systems into national ones with limited resource
- Some exceptions, e.g., Brazil
- Lack of major scientific research programs until Brazil, China, India in 1980s
- Diverging Vaccination coverage:
  - Industrialized countries: 60 %
  - Latin America: 38 %
  - South Asia: 5 %
  - East Asia: 5 %
  - Middle East: 25 %
  - Sub-Sahara Africa: 5 %

Increased Demand, Increased Cost, Increased Regulations and Price Pressure

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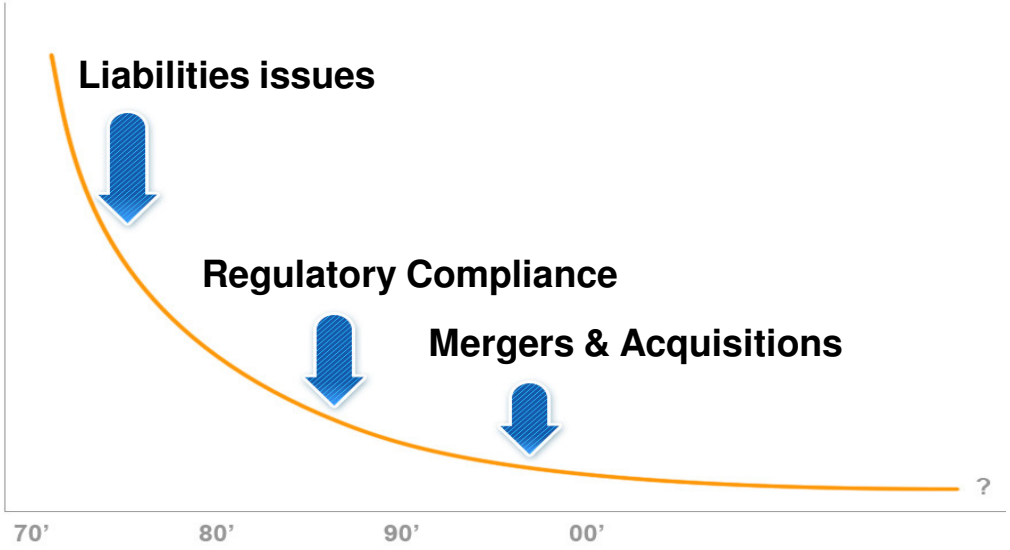
- Global programs required increased supply at minimum cost/profit
- Increasing costs of R&D, quality and production
- EPI/UNICEF faced severe shortages and high prices as suppliers merged and reached capacity limits during 1990s
- 10 of 14 developed-world manufacturers partially or totally stopped production of traditional vaccines during 1998-2001 (UNICEF)

Number of Developed-World Vaccine Manufacturers



4. Contemporary Era: Privatization and Biotechnology (~1990 ➡)

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- Small Number of Large Producers and emerging or re-emerging smaller producers who have to bear increased and/or increasing
  - Costs of Research and Development
  - Costs of Production facilities
  - Risks of litigation
  - Shareholder growth/profit expectations (otherwise risk to invest into other sectors)

Importance of a Solid R&D-Based Industry

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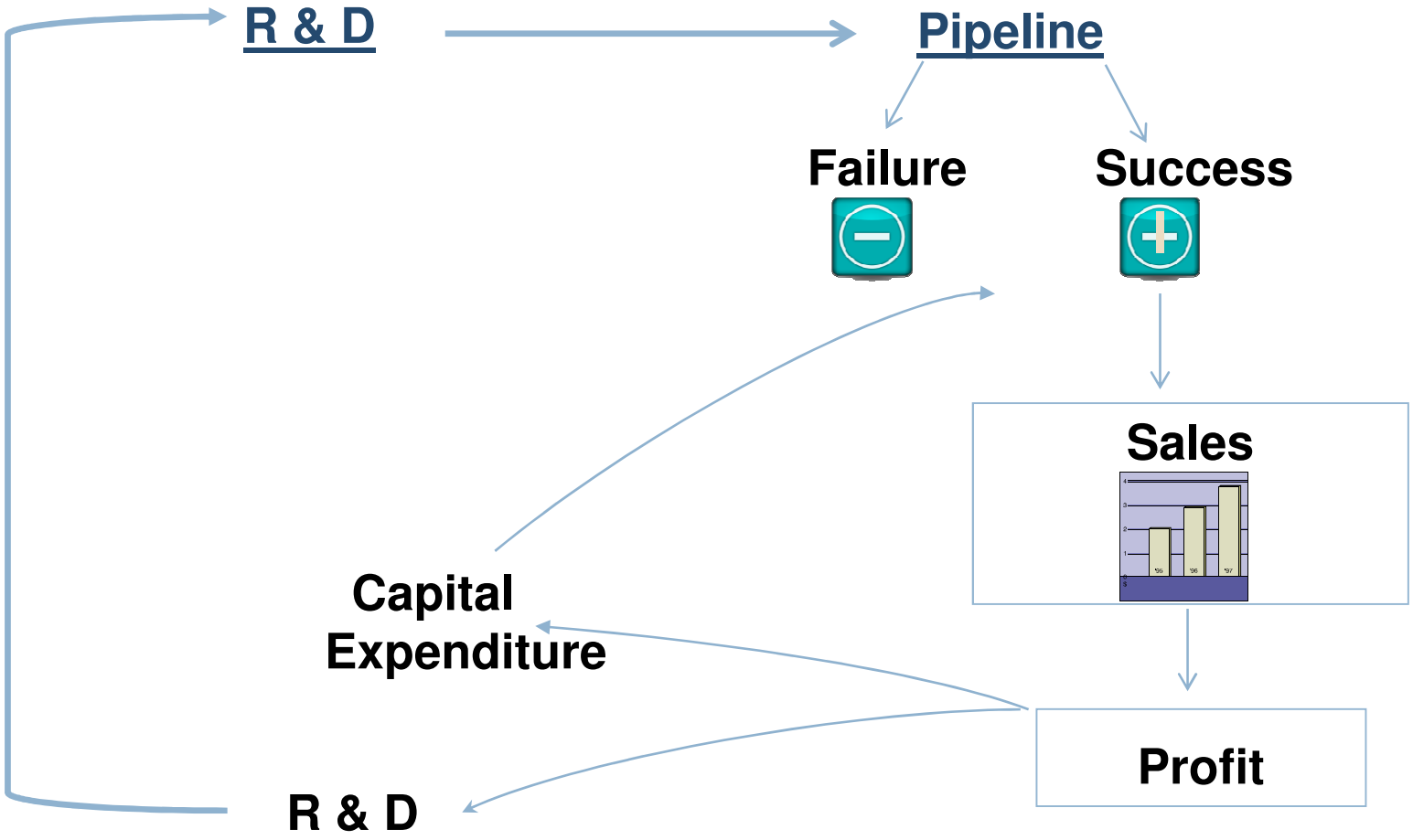
Pipeline diversification increases chances of success



Research & Development Cycle

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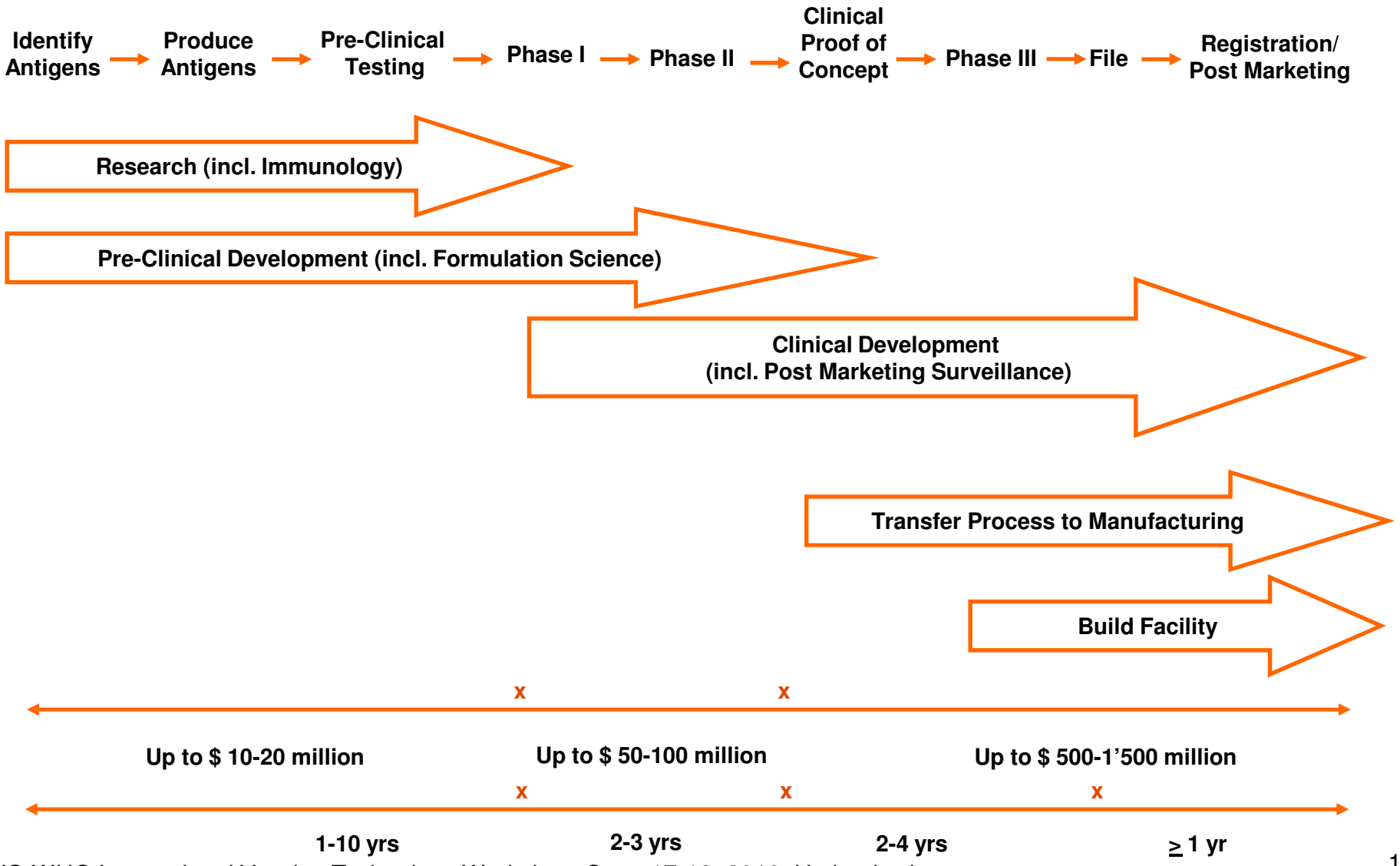

Key Considerations for Technology Transfer Today

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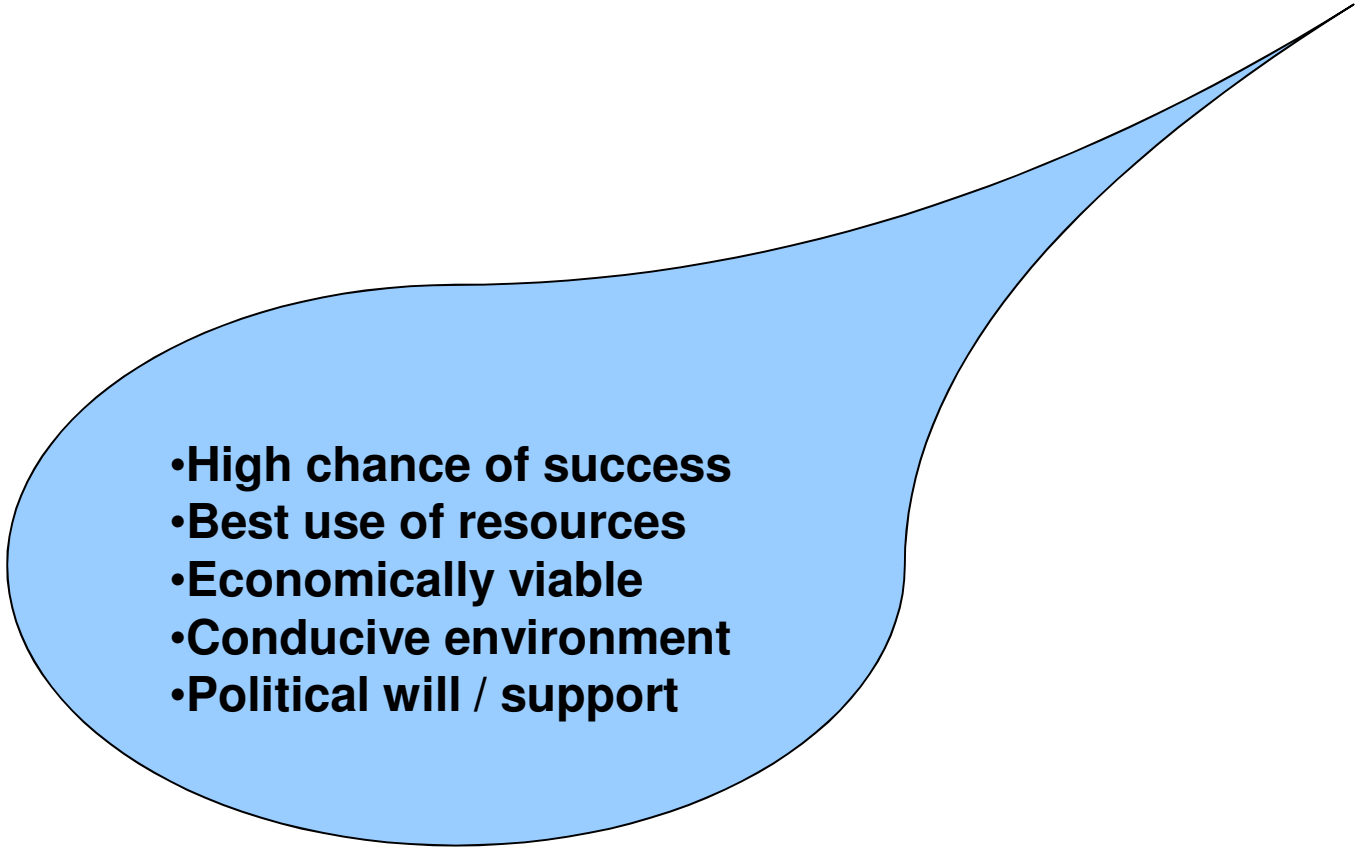

Tech Transfer is a Long, Expensive and Risky Exercise (no quick fix)

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It requires

- At least two committed partners (ultimately to reach similar expertise level)
- Stable political climate (sustainable commitment)
- A 5-10 yrs process
- $ hundreds of million (from somewhere)
- Skilled workers (or trainable workers) to carry out R&D and high-tech manufacturing
- A supportive regulatory environment (stringent quality, safety and efficacy criteria)
- An independent Official Medicines Control Laboratory (no double standard)
- Strong political will and commitment (demonstrated by prioritization of immunization in health budget)
- Appropriate Intellectual property (IP) protection
- A predictable commercial environment (economy of scale)
- Assurance it will really improve access and/or decrease cost/price

Tech transfer applies usually to "mature" technologies (experience is prerequisite)

In addition,

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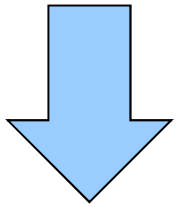
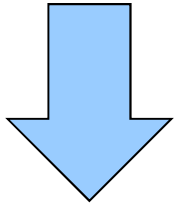
A stepwise progression of tech transfer is preferred:

Packaging and distribution



Bulk transfer, fill and finish



Bulk production

Fools rush in where angels fear to tread: Stepwise Approach to Tech Transfer in Vaccines

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A stepwise approach securing downstream processes prior to developing bulk production capacity

Phase 1

Packaging and Distribution of Finished Product

Implementation of :

- Basic Quality Control
- Labeling
- Cold chain
- Distribution network
- Adverse event reporting
- …

Phase 2

Phase 1 Plus Filling of Bulk

Implementation of :

- Sterile filling unit
- Sterility assurance
- QC expertise
- Validated suppliers
- Quality Assurance
- …

Phase 3

Phase 2 Plus Production of Active Principle

Implementation of :

- Engineering
- Bulk production expertise
- Sustainability
- Economic viability
- …

Examples of Vaccine Tech Transfer and Joint Venture Programs

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Partners	Types of vaccines
Bharat Biotech (India) – Wyeth (Pfizer)	Hib
Bio Farma (India) – Biken	polio, measles
Bio Kangtai (China) – sanofi pateur	JE, influenza
Bio Manguinhos (Brazil) – Biken	Measles, polio, rubella
Bio Manguinhos (Brazil) – GSK Bio	Hib, MMR, OPV, pneumococcal conjugate, Rotavirus
Biological E (India) – Intercell	JE
Birmex (Mexico) – sanofi pasteur	influenza
Butantan (Brazil) – sanofi pasteur	influenza
China – GSK	Various vaccines, including influenza
China – Merck	HepB
Egypt - GSK	DTP-HepB, MMR, Meningitis, OPV
India - GSK	Various vaccines
India - Novartis	rabies
Panacea Biotech (India) – Novartis	DTP-Hib
Russia – GSK	Various vaccines
Thailand – Merck (Nobilon)	influenza
Ukraine – GSK	MMR

Technology Transfer & Local Production is Ongoing for Influenza Vaccines

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COUNTRY	PRODUCTION INITIATIVE	COMPANY
Brazil (Sept 2009)	Agreement with Butantan to produce and supply pandemic influenza H1N1 vaccines to Brazilian government; vaccine formulation, filling and packing in Brazil	sanofi pasteur
Mexico (Mar 2009)	Agreement to build a facility to manufacture seasonal and pandemic influenza vaccines in collaboration with Birmex, a Mexican federal vaccine manufacturer	sanofi pasteur
WHO / Thailand (Feb 2009)	License granted to WHO for egg-based seasonal and pandemic live-attenuated influenza vaccine technology; WHO to sub-license to developing country public sector vaccine manufacturers; Thailand is the 1st country to request sub-license	Merck & Co. (Nobilon)
China, Hong Kong & Macau (Nov 2008 / June 09)	Joint venture agreement with Shenzhen Neptunus Interlong Bio-Technique Co Ltd to develop & manufacture seasonal influenza vaccines and pre-pandemic / pandemic influenza vaccines	GSKBio
China (Nov 2007)	Agreement with the Chinese authorities to build a facility to manufacture seasonal and pandemic influenza vaccines	sanofi pasteur
Indonesia	Agreement with Bio Farma to build a facility to manufacture seasonal influenza vaccines	Biken
Brazil (1999)	Agreement with Butantan to build a facility to manufacture seasonal influenza vaccines	sanofi pasteur

GSK – FIOCRUZ

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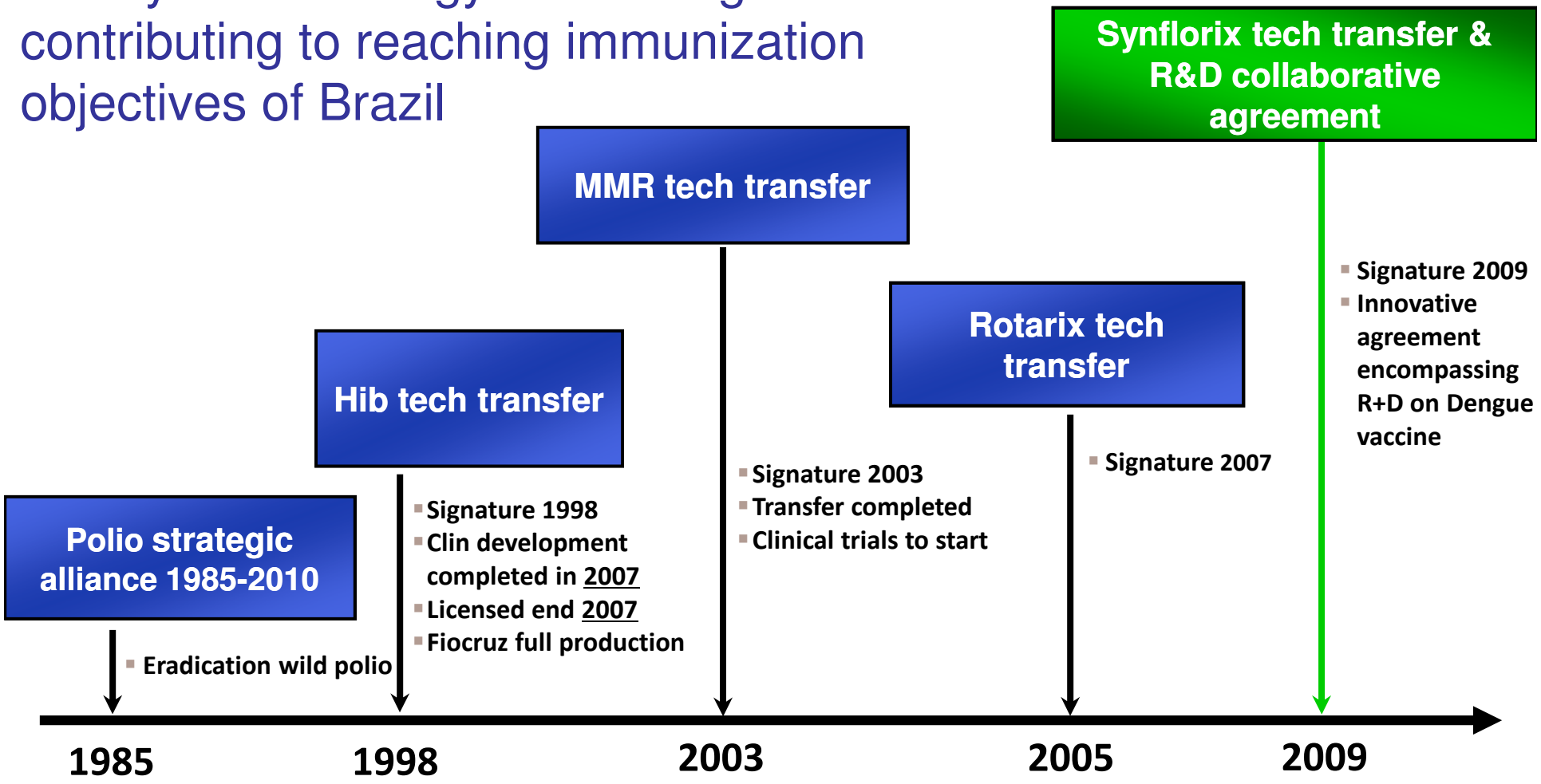
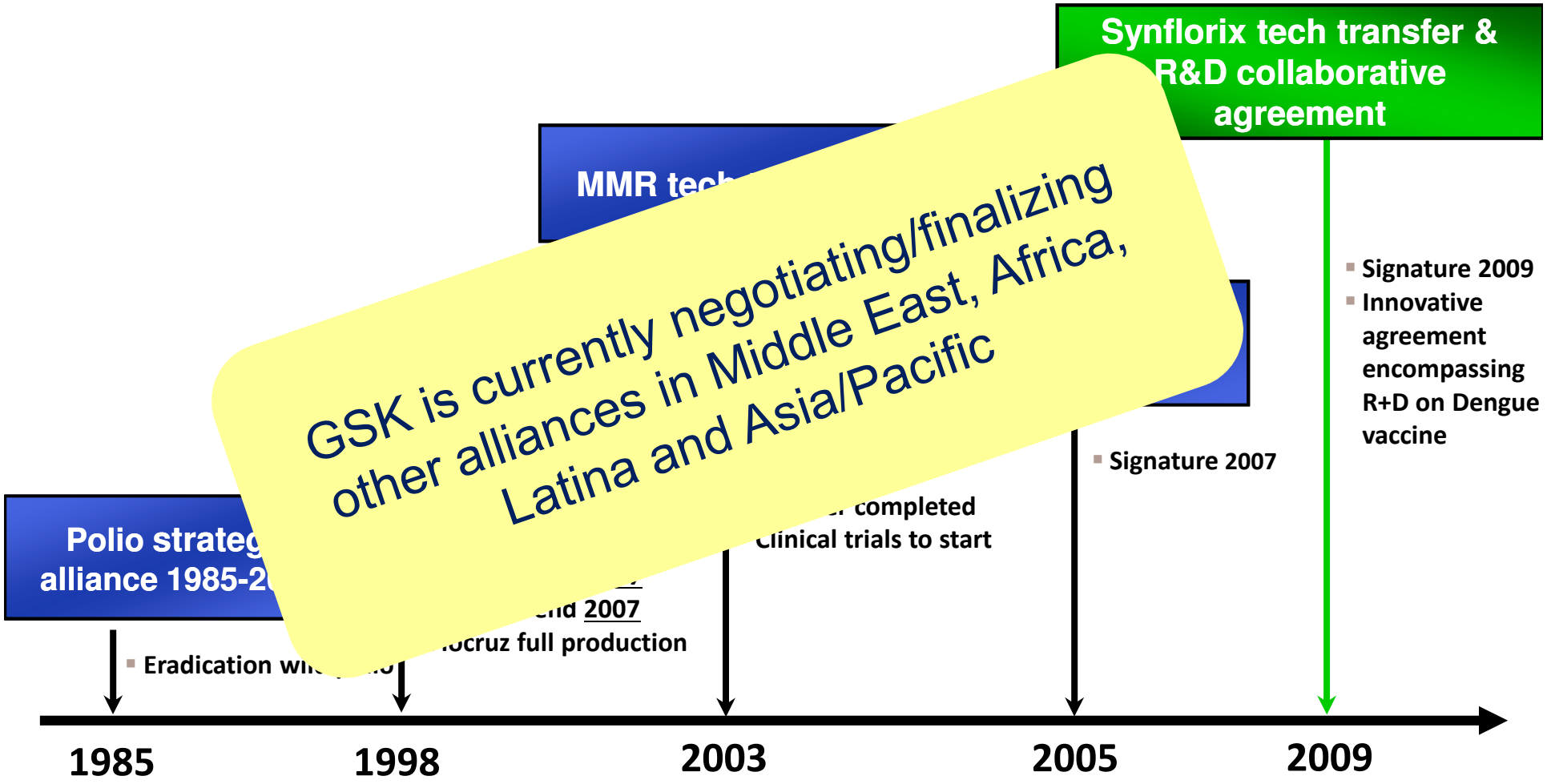
history of technology transfer agreements contributing to reaching immunization objectives of Brazil



GSK - FIOCRUZ



GSK is currently negotiating/finalizing other alliances in Middle East, Africa, Latina and Asia/Pacific

Conclusions: Sustainable Vaccine Production

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- Tech Transfer is not the only factor that determines access to care and vaccines
- Industry is not opposed to Tech Transfer, but it must be voluntary: requires 2 committed partners
- Tech Transfer can only be considered by the R&D-based industry when the conditions for success are met
- In many circumstances, for very good reasons tech transfer is not possible, in this case the R&D-based industry ensures access to vaccines though the tiered pricing mechanism
- Maintaining a free and healthy market is key to ensure the sustainability of innovation and affordability of vaccines